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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,500	07/24/2006	H. Scott Roderick	ABLE-0027	9312

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EXAMINER	
ARIANI, KADE	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/561,500	RODERICK ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-63* is/are rejected.

7)☒ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed on December 19, 2005, has been received and entered.

Claims 1-29 have been canceled.

Claims 30-63 are pending in this application and were examined on their merits.

Claim Objection

Claims 30, 38-40 are objected to because of the following informalities:

The use of function word "the" in claim 30 is incorrect, because the "composition" has not been previously specified. Appropriate correction is required.

Claims 38-40 are objected to as being an improper dependent claim, because claim 38 does not refer to a preceding claim and refers to itself, also claims 39 and 40 are objected to since they are dependent on claim 38.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44-46 recite the limitation "nucleic acid". There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999, p.221-226).

Claims 30-34, 37 are drawn to a composition comprising a sponge toxin, sponge toxin comprises poly-APS, sponge toxin is obtained form *Reniera sarai*, wherein the sponge toxin has a molecular weight between 5.0 kDa to 20 kDa.

Malovrh et al. disclose a composition comprising a sponge toxin, sponge toxin comprises poly-APS, sponge toxin is obtained form *Reniera sarai*, wherein the sponge toxin has a molecular weight between 5.0 kDa to 20 kDa (p. 221, Abstract and Introduction 1st column, p. 222 Fig.1a.).

Malovrh et al. therefore clearly anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30-40, and 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999, p.221-226).

Claims 30-40, and 60-63 are drawn to a composition comprising a sponge toxin, sponge toxin comprises poly-APS, sponge toxin is obtained form *Reniera sarai*, wherein the sponge toxin has a molecular weight between 5.0 kDa to 20 kDa, the concentration of sponge toxin is between 0.5 ng/ml and 0.5 µg/ml, and a method for reversible formation of membrane pores, comprising the steps of a) incubating the membrane in the presence of composition comprising a sponge toxin, b) removing the composition from contact with the membrane, and addition of zinc solution (concentration is between 1 to 2 mM, 1.5mM).

Malovrh et al. teach a composition comprising a sponge toxin, sponge toxin comprises poly-APS, sponge toxin is obtained form *Reniera sarai*, wherein the sponge toxin has a molecular weight between 5.0 kDa to 20 kDa, the concentration of sponge toxin is between 0.5 ng/ml and 0.5 µg/ml (p. 221, Abstract and Introduction 1st column, p. 222 Fig.1a., and p.223 Fig.3.).

Malovrh et al. further teach a method for the reversible formation of membrane pores, comprising the steps of incubating the membrane in the presence of composition comprising a sponge toxin, and addition of zinc solution, the concentration of zinc solution is between 0 to 1 mM (p.222 1st column, 2.2, and 2nd column 4th paragraph 2.5.).

Malovrh et al. is silent about removing the composition from contact with the membrane. However, removing a substrate from a reaction mixture is within the capability of a person with ordinary skill in the art.

Thus, it would have been obvious to one of ordinary skill in the art to modify the method as taught by Malovrh et al. by adding a step of removing the composition comprising sponge toxin from the contact with the membrane and provide a method for reversible pore formation The motivation would be to control the degree of pore formation by sponge toxin in the membranes.

Claims 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woude et al. (in IDS, PNAS, 1997, Vol. 94, p.1160-1165) in view of Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999, p.221-226).

Claims 41-49 are drawn to a method for transfection of a macromolecule into a cell *in vitro*, the method comprising the steps of: a) incubating the cell in the presence of a composition comprising a sponge toxin, b) removing the composition from contact with the cell; and c) adding a macromolecule, the macromolecule is cDNA, the cell is incubated in the presence of the composition for 5 minutes, prior to the addition of the macromolecule, the composition and macromolecules are removed and replaced with standard media, cells are incubated for 180 minute.

Woude et al. teach a method for transfection of a macromolecule into a cell *in vitro*, comprising the steps of: a) incubating the cell in the presence of a composition comprising a pyridinium compound, removing the composition from contact with the

cell, adding a macromolecule, the macromolecule is cDNA, prior to the addition of the macromolecule, the composition and macromolecules are removed and replaced with standard media (Abstract and p.1161, 2nd column 5th paragraph).

Woude et al. further teach pyridinium compounds have been developed that display highly efficient DNA transfection properties. The transfection efficiency of several of these compounds is enhanced by an order of magnitude when compared with the transfection efficiency accomplished with the widely used cationic lipid system, lipofectin. Most importantly, the pyridinium compounds were found to be essentially nontoxic toward cells (Abstract).

Woude et al. do not teach transfection in the presence of poly-APS (pyridinium compound), and the claimed incubation times. However, Malovrh et al. teach a composition comprising a sponge toxin, a pyridinum compound, polymeric alkylpyridinium (poly-APS), obtained form *Reniera sarai*. Malovrh et al. further teach the hemolytic activity of poly-APS is due their detergent-like structure and behavior in aqueous solutions.

Moreover, routine experimentation is widely used by one of ordinary skill in the art to determine optimum or workable ranges of particular parameters such as incubation time, and concentration of reagents in a transfection assay. "[W] here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP Chapter 2100 – p.141).

Therefore, it would have been obvious to one of ordinary skill in the art to substitute the pyridinium compound in the transfection method as taught by Woude et

al. with the pyridinium compound (poly-APS) as taught by Malovrh et al. to achieve a method for transfection of a macromolecule into a cell *in vitro*, because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Claims 50-59 are rejected are rejected under 35 U.S.C. 103(a) as being unpatentable over Woude et al. (PNAS, 1997, Vol. 94, p.1160-1165) and Arendt et al. (Neuroscience, 1998, Vol. 85, No.4, p.1337-1340) in view of Ballard C.G. (European Neurology, 2002, Vol. 47, p.64-70) and further in view of Bunc et al. (Toxicon, 2002, Vol. 40, p.843-849).

Claims 50-53 are drawn to a method for transfection of a macromolecule into a cell *in vivo*, the method comprising the steps of: a) incubating the cell in the presence of a composition comprising a sponge toxin and a macromolecule, the macromolecule is the cytoskeletal protein tau, and hippocampal neurone.

Claims 54-59 are drawn to a rodent model and a method of studying a neurological disease comprising applying a composition comprising a sponge toxin, tau protein, and phosphatase inhibitor, to the hippocampus of a rodent, the phosphatase inhibitor is okadaic acid.

As mentioned immediately above, Woude et al. teach a method for transfection of a macromolecule into a cell using pyridinium compounds.

Woude et al. further teach oligonucleotide and /or gene therapy are promising approaches not only in the treatment of diseases with a genetic defect, but also in developing therapeutic strategies for diseases such as cancer, infectious disease, and

acquired diseases. Vesicles composed of cationic synthetic amphiphiles have been developed for the delivery of genes *in vitro,* as well as *in vivo*. Nucleic acids associate with amphiphiles in a highly efficient manner, and protocols for preparation and delivery are simple, the transfection efficiencies are usually better, however, a major drawback of synthetic amphiphiles has been the severe cellular toxicity of such compounds (p. 1160 Introduction 1st and 2nd columns).

Woude et al. do not teach sponge toxin (poly-APS). However, Bunc et al. teach effects of poly-APS isolated from *Reniera sarai*, in rat. Bunc et al. also teach, poly-APS is a potent acetylcholinesterase inhibitor, and the acetylcholinesterase inhibitory effects are not responsible for the lethal activity of the toxin (Abstract and p.847, 1st column lines 2-5).

Woude et al. do not teach the cytoskeletal protein tau, and hippocampal neurone. However, Arendt et al. teach a rodent model and a method of studying a neurological disease comprising applying okadaic acid to the cerebral cortex of a rodent (p.1337, 2nd column, p.1338, 1st column and Fig.1.).

Arendt et al. further teach one major abnormalities in AD are made up by the microtubule-associated protein tau in a hyperphosphorylated form(p.1337, 1st column).

Arendt et al. also teach okadaic acid applied either by single local injection or by chronic intraventicular infusin into rat brain induces a hypephosphorylated state of tau at some of those sites that are found to be hyperphosphorylated in tau preparation obtained from Alzheimer's disease (AD) brains (p.1337, 2nd column 3rd paragraph).

Further motivation is in, Ballard who teaches therapeutic approaches in the treatment of Alzheimer's disease (AD) were developed with the aim of enhancing

cholinergic function, the most successful of which has been the use of cholinesterase inhibitors (Abstract tan dp.65, 1st column 2nd paragraph).

Therefore, in view of the above teachings, it would have been obvious to one of ordinary skill in the art to substitute the transfection agent in the transfection method of Woude et al. with a composition comprising sponge toxin (pyridinium compound) as taught by Bunc et al. to provide a method for transfection of a macromolecule *in vivo*, because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Moreover, since, at the time the invention was made it was well known in the art that among the therapeutic approaches in the treatment of Alzheimer's disease (AD) the use of cholinesterase inhibitors has been the most successful thus, a person of ordinary skill would have been motivated to modify the method of Arendt et al. by applying a sponge toxin, a potent acetylcholinesterase inhibitor, as taught by Bunc et al. to provide a method of studying a neurological disease.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Kade Ariani
Examiner
Art Unit 1651